

-continued

gtcatcgata	acatccctgtc	caagatcgag	aacgagtagcg	aggtgctgtc	ctcgaaagcc	120
ctggccaggag	tctacaggag	cctgaaagag	cgctggaga	acaacgtgtat	gacccttcaac	180
gtgaaacgtgt	aggatatcc	gacacgagg	ttaacaaga	gggagaactt	caagaacgtgt	240
ctggaaagagcg	atctgtatcc	ctacaaagat	ctggaaacca	gcacactacgt	gttcaaaat	300
ccctacaatgt	tcttgaacaa	gggaaagaga	gataaagtcc	ttggcaggta	caattacatc	360
aaggatagca	tgtacacccgt	tatcaaaatgt	ggcaaaatgt	tcttgggata	cttacaaatgt	420
ctgtccggaa	agtacaaatcg	cgatctggat	agcatcaaga	agtatcatca	cgataaagcg	480
ggggaaagacgg	agaagttacat	ggccatctgt	aaacaaatcg	agacccctgt	caagaaacgtc	540
aaacgatataaa	tgtatgtgt	cgtgtatccc	ctggaaaggca	aggctctgtc	gttacatcat	600
gagaagagca	acgtgggggt	caagatcaat	gagctgtttat	acctgtaaag	catccaggat	660
aaatgtggcg	atttcaaaatg	aaacaaacaa	tttcgttggaa	tccggatct	gagccacccgt	720
tacaaccaca	acaacactgt	gaccaatgtt	ctggcaccgt	gaatgttgc	cgaaaaacgt	780
ggccaaagacgg	tctgtggacaa	ctctgtggat	ggaaacactgt	aggaaatgtt	gttacatgtcg	840
cgccacccatgt	gttgcggaa	gttgcgttcc	cgacaaacacgt	gttgcgttcc	acacccgtgt	900
gaggaggagg	atgtcaatgt	ctctgtgtac	tacaaacgg	aggagatata	gttgcgttgc	960
aacccaaatct	ctacttgtaa	cgacaaatgt	gggatgtgc	atccggatgt	caatgttacc	1020
gaggaggatt	cggaaacaa	cgggaaagaa	atccatcggt	atgttaccaa	gttgcgttgc	1080
tatccactgt	tgtatgttat	tttctgtgt	cacccacccaa	accacccacta	actcgaggat	1140
cc						1142

What is claimed is:

1. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding wild-type merozoite surface protein (MSP-1) operably linked to a mammary gland promoter,

wherein the modification reduces the AT content of SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon, and

wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

2. The mammal of claim 1, wherein the promoter is a β -casein promoter.

3. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

4. The mammal of claim 3, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

5. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

6. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

7. The mammal of claim 1, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 181 and 263.

8. A method of producing a merozoite surface protein 1 (MSP-1) in the milk of a non-human transgenic mammal, comprising:

35 providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding wild-type MSP-1 operably linked to a mammary gland promoter, wherein the modification reduces the AT content of SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

9. The method of claim 8, wherein the promoter is a β -casein promoter.

10. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

11. The method of claim 10, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

12. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

13. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

14. The method of claim 8, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 181 and 263.

15. A non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter,

wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon, and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby produce MSP-1 in its milk.

16. The mammal of claim 15, wherein the promoter is a β -casein promoter.

17. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

18. The mammal of claim 17, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

19. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

20. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

21. The mammal of claim 15, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising amino acid substitutions at positions 182 and 263.

22. A method of producing a merozoite surface protein 1 (MSP-1) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter, wherein the modification eliminates all the mRNA instability motifs in said SEQ ID NO: 2 by replacement of protozoan codons with codons preferred by mammalian cells, and wherein the replacement codons encode the same amino acid as the replaced codon; and, allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-1 in its milk.

23. The method of claim 22, wherein the promoter is a β -casein promoter.

24. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks at least one glycosylation site.

25. The method of claim 24, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid sequence that lacks all glycosylation sites.

26. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

27. The method of claim 22, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

28. A transgenic non-human mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland specific promoter, wherein the modification eliminates all the mRNA instability motifs of said SEQ ID NO: 2 by replacement of one or more protozoan codons with codons preferred by mammalian cells and the modification reduces the AT content of said SEQ ID NO: 2 by 50% or less by replacement of protozoan codons with codons preferred by mammalian cells, wherein the replacement codons encode the same amino acid as the replaced codon and wherein the transgenic mammal expresses said modified SEQ ID NO: 2, thereby to produce MSP-1 in its milk.

29. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

30. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

31. The mammal of claim 28, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

32. The mammal of claim 28, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

33. The mammal of claim 28, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

34. The mammal of claim 28, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

35. The mammal of claim 28, wherein the promoter is a β -casein promoter.

36. A method for producing a merozoite surface protein 1 (MSP-1) sequence in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified SEQ ID NO: 2 encoding a wild-type MSP-1 operably linked to a mammary gland promoter, wherein the nucleic acid has been modified by a) elimination of mRNA instability motifs by the replacement of protozoan codons in SEQ ID NO: 2 with codons preferred by mammalian cells; and

b) reduction of AT content by 50% or less by the replacement of one or more AT-containing protozoan codons of SEQ ID NO: 2 with codons preferred by mammalian cells,

wherein the replacement codons encode the same amino acid as the replaced codon; and

allowing the transgenic mammal to express said modified SEQ ID NO: 2, to thereby produce MSP-1 in its milk.

37. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 25% more than the wild-type sequence is expressed under the same conditions.

38. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

39. The method of claim 36, wherein the modified SEQ ID NO: 2 is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

40. The method of claim 36, wherein all protozoan codons are replaced with codons preferred by mammalian cells.

41. The method of claim 36, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 182.

42. The method of claim 36, wherein the modified SEQ ID NO: 2 encodes an MSP-1 comprising an amino acid substitution at position 263.

43. The method of claim 36, wherein the promoter is a β -casein promoter.